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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/734,443	10/17/96	KEYT	B A-63096/WHD

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EXAMINER

SAUD, C

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 07/09/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

08/734,443

Applicant(s)

KEYT et al.

Examiner

Christine Saoud

Art Unit

1647



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 21, 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 7-14 is/are rejected.
- 7) ☒ Claim(s) 5 and 6 is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

Art Unit: 1646

DETAILED ACTION

Response to Amendment

1. Claims 1-14 are pending in the instant application.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.
4. Applicant's arguments filed 21 May 2001 have been fully considered but they are not deemed to be persuasive.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3 and 7-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for substitution with aspartic acid, does not reasonably provide enablement for any amino acid modification as encompassed by the claims. The specification does

Art Unit: 1646

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the reasons of record in paper #26.

Applicant argues that "the present disclosure, along with the general knowledge in the field, fully enables the skilled artisan to make and use the claimed invention without undue experimentation. This argument is not persuasive and is not supported by any facts of record. As stated previously, the prior art of record identifies VEGF mutants which meet the structural limitations of the instant claims as well as teaching substitution of cysteine residues in VEGF with serine. The prior art specifically exemplifies the cysteine residues of the instant claims (see Claffey and Potgens). Applicant has argued that the mutant VEGF proteins of Potgens are not antagonistic, which is confirmed by Potgens at page 32884, column 2, paragraph 3. However, this evidence also shows that the instant claims are not enabled for their full breadth. The instant specification discloses mutation of the cysteine residues (specifically at positions 51 and/or 60) to aspartic acid result in an antagonistic molecule. This result is unexpected based on the teachings of Potgens. Because this result is unexpected, claims limited to this substitution are not anticipated or made obvious by the prior art. However, these results cannot serve as a basis for enablement of the broad claim, because evidence of Potgens demonstrates that not each and every amino acid substitution or amino acid modification will result in an antagonist. It is not clear which amino acid substitutions or amino acid modifications would provide for the desired biological activity. Furthermore, a single substitution is not predictive nor should it serve as a

Art Unit: 1646

basis for the broad claim when the art specifically teaches another substitution encompassed by the claim which clearly is inoperative. The specification only provides guidance for aspartic acid substitution and the art would suggest that it would be unpredictable to substitute other amino acids in light of the result with serine substitution. Therefore, the experimentation that would be required to practice the full breadth of the claims would be undue because one would not have a reasonable expectation of making a substitution or modification, expect for the substitution of aspartic acid, and obtain a functional protein with the required biological activity.

Applicant argues that the disclosure "gives substantial direction as to the importance of the different cysteine residues VEGF in making the claimed variants". However, the rejection is based on the lack of guidance for which substitutions should be made at the cysteine residues to result in the claimed antagonistic molecules. Applicant further argues Wands, however, a complete Wands analysis of the claimed invention was made, and it was concluded that the experimentation required to practice the invention would not be routine, but rather, undue in light of the lack of guidance, the lack of evidence, the state of the art at the time of the invention, the amount of experimentation required and the lack of predictability in the art.

Applicant argues at page 7 of the response that substitutions could be made and the resultant protein could be tested for biological activity. However, this is merely an invitation to experiment. Such a suggestion is found in Potgens (see page 32884, column 2, paragraph 3), however, this cannot serve as a basis for a rejection over the prior art and it therefore, cannot serve as a basis for allowance of the generic claim either. Applicant again argues that a working

Art Unit: 1646

example is provided, however, a single data point is not representative of the breadth of what is being claimed and further, a single species can rarely serve as a basis for a generic claim (see *In re Clarke*, 148 USPQ 665, (CCPA 1966)).

Conclusion

7. Claims 5-6 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Art Unit: 1646

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud, Ph.D., whose telephone number is (703) 305-7519. The examiner can normally be reached on Monday to Friday from 7AM to 3PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556. If this number is out of service, please call the Group receptionist for an alternate number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

July 3, 2001

**CHRISTINE J. SAOUD
PRIMARY EXAMINER**

Christine J. Saoud